May 30, 2002

Sarah C. Loftus
American Chemistry Council Petroleum Additives Panel
Health, Environmental and Regulatory Task Group
1300 Wilson Blvd.
Arlington, VA 22209

Dear Ms. Loftus:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Alkaryl Sulfonates category, posted on the ChemRTK HPV Challenge Program Web site on November 30, 2001. I commend The American Chemistry Council Petroleum Additives Panel, Health, Environmental and Regulatory Task Group for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its HPV Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the attached Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The American Chemistry Council Petroleum Additives Panel Health, Environmental and Regulatory Task Group advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
A. Abramson
C. Auer
M. E. Weber

EPA COMMENTS ON CHEMICAL RTK HPV CHALLENGE SUBMISSION:
PETROLEUM ADDITIVE ALKARYL SULFONATES CATEGORY

SUMMARY OF EPA COMMENTS

The sponsor, American Chemistry Council Petroleum Additives Panel, Health, Environmental, and Regulatory Task Group (HERTG), submitted a test plan and robust summaries to EPA for the petroleum additive alkaryl sulfonates category dated October 10, 2001. EPA posted the submission on the ChemRTK HPV Challenge Web site on November 30, 2001.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The submitter's justification for grouping the category members is not sufficient to fully evaluate the test plan. EPA requests additional information on the total composition of each CAS number to be tested including the average chain length of each chemical, and information on whether the synthetic alkaryl sulfonates contain a petroleum diluent. If the composition varies, then the submitter should provide typical compositions or composition ranges.

2. Physicochemical and Environmental Fate Data. (a) The submitter needs to provide robust summaries for octanol-water partition coefficient and water solubility. (b) The submitter needs to resolve some inconsistencies in the biodegradation Test Plan and robust summaries.

3. Health Endpoints. (a) The submitter needs to prepare a more detailed justification for adequacy of existing data, based on the toxicokinetic and physicochemical properties of category members. (b) The submitter proposed additional testing for repeated-dose toxicity, reproductive toxicity, and developmental toxicity on one category member (CAS no.115733-09-0; C14-C24 alkaryl calcium salt). Although this test plan appears to adequately address SIDS-level health effects endpoints, the submitter needs to provide a clear and more complete justification for use of a single test substance to characterize the reproductive and developmental toxicity of the remaining 11 members of the category. (c) The submitter needs to address deficiencies in the robust summaries.

4. Ecotoxicity. (a) EPA agrees with the proposed ecological effects testing in fish, invertebrates, and algae, but prefers that test methods follow more closely the OECD's Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (Ref. 1). (b) The submitter indicated that adequate data are available from existing acute aquatic studies using nominal concentrations and water-accommodated fractions (WAFs). The submitter's justification for using these studies as supporting information is inadequate (see Specific Comments on the Robust Summaries). (c) EPA recommends conditional chronic invertebrate toxicity testing (see Test Plan.)

EPA requests that the Submitter advise the Agency within 90 days of any modifications to its submission.

EPA COMMENTS ON PETROLEUM ADDITIVE ALKARYL SULFONATES CATEGORY CHALLENGE SUBMISSION

Category Definition

The petroleum additive alkaryl sulfonates category contains benzenesulfonic acids that are substituted with one or more saturated linear and/or branched alkyl groups of varying length and are used as petroleum additives in petroleum base stocks.

The substances in this category are covered under 12 broadly defined CAS numbers that differ with respect to the source material used in their manufacture, the number and chain length of the alkyl substituents, the

counter-ion in the sulfonic acid salts, and their complexation ("overbase" formation) with calcium carbonate. Although it is not stated in the test plan, many commercial products with different chemical compositions could be marketed for any one CAS number, and it is likely that a single commercial product will vary in chemical composition from batch to batch. This is especially likely for the petroleum-derived products where there is a high natural variability in the starting materials. The petroleum additive alkaryl sulfonates in this category are marketed as the free acids (CAS Nos. 71549-79-6 and 115829-36-2); salts of sodium, calcium, barium, and magnesium; or the "overbased derivative" calcium salt complex.

Petroleum additive alkaryl sulfonates are produced from the sulfonation of either synthetic alkylbenzene substrates or naturally occurring alkylaromatic-rich fractions of heavy lubricating oil base stocks. The test plan suggests that alkaryl sulfonates produced from synthetic alkylbenzenes will be distinctly different than those produced from heavy lubricating oil base stock, as the latter will contain unsulfonated alkanes in addition to the mixed alkylated benzenesulfonic acids. However, although the submitter states that the petroleum additive alkaryl sulfonates are manufactured in petroleum base stocks, and thus are never isolated, it is not clear from the test plan whether the synthetic alkaryl sulfonates likewise contain a petroleum diluent. Without clarification of this point EPA cannot fully evaluate the test plan.

Category Justification

The submitter bases this category on the members' structural similarity, their similar physicochemical properties, and their similar aquatic and mammalian toxicities. However, more information is needed on the petroleum additive content in each substance and whether a CAS number represents the named substance or the substance plus diluent.

In the descriptions of the planned testing, the submitter develops the following important subcategories specific to the endpoints under consideration: (1) petroleum-derived salts; (2) synthetic alkylbenzene-derived salts; and (3) synthetic alkylbenzene-derived acids.

The limited available physicochemical data and a discussion based on structure support the submitter's conclusion that the members of the category exhibit similar physicochemical properties. All of the members have or are likely to have low water solubilities, high octanol/water partition coefficients, and low vapor pressures. EPA believes that these chemicals may be more water dispersible than soluble in water, which increases the concern for their potential toxicity to aquatic organisms.

The submitter discusses the likelihood that the members of this category will resist hydrolysis and direct photolysis. For biodegradation, the test plan reasonably divides the alkaryl sulfonates into three subgroups to more closely match specific substructural aspects of the alkaryl sulfonates that are important in assessing biodegradation. Single members from two of the three subgroups (mixed linear and branched alkyl side chains and petroleum-derived substances) had similar degradation rates.

In support of treating alkaryl sulfonates as a single group for mammalian toxicity testing purposes, the submitter notes that the sulfonic acid moiety on an aromatic ring represents the only functional group that may have biological activity. The submitter further notes that despite the low water solubility of these substances, members with the shortest alkyl side chains are the most likely to penetrate biological membranes and the most likely to be distributed in the systemic circulation and possibly reach a potential target organ. The test plan focuses on chain length as the key structural variable, with characterization of substances at the upper and lower limits for chain length in the category for most endpoints. Although alkyl side chain branching is also a structural variable for this category, its potential influence on toxicity is not addressed in the human health effects section of the test plan.

The submitted test plan may be adequate to characterize the human health effects of the category, provided that the submitter can prepare a clear and more complete justification for the proposed approach. The test

plan provides only relatively brief discussion on the toxicokinetic properties of category members in Section 4.3.1 of the test plan. This discussion needs to be expanded using data from the cited references to address key issues such as the comparative absorption, tissue distribution, and metabolism of category members in mammals and potential variation in these properties resulting from differences in alkyl chain length or branching.

For ecological effects testing, the petroleum additive alkaryl sulfonates are grouped into four subcategories by substructural features, such as alkyl side chain length, that are important in assessing ecotoxicity. While this is a reasonable approach, it is important to know the average chain length and the presence of petroleum additive in each category member to fully assess the adequacy of the ecotoxicity data.

Test Plan

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The submitter's approach for melting point, boiling point, vapor pressure, Log P (octanol-water partition coefficient), and water solubility is acceptable for the purposes of the U.S. HPV Challenge Program. However, the submitter needs to provide robust summaries in order to support the octanol-water partition coefficient and water solubility data it provided in Table 3 of the Test Plan (page 35).

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The submitter's approach for photodegradation, stability in water, and biodegradation is acceptable for the purposes of the HPV Challenge Program. However, the submitter needs to address some inconsistencies found in the biodegradation robust summaries.

Biodegradation. In Table 4 of the Test Plan (page 36) the following inconsistency was noted: robust summaries and data are available for CAS Nos. 68783-96-0 (page 11 of the RS), and 71786-47-5 (page 6 of the RS); however, for these compounds "No testing needed, Bridging" is entered in the table. The results for biodegradability of these two compounds also need to be entered in Table 4. In the robust summary 3 for analog of CAS No. 70024-69-0, detailed information on the biodegradability test for an unrelated substance, CAS No. 68511-50-2, is also included on page 9. The submitter needs to correct the summary, and the Test Plan, if appropriate. It is unclear whether the results are for the analog of CAS No. 70024-69-0 or for CAS No. 68511-50-2.

Fugacity. The submitter indicates in the Test Plan (page 12) that it will use estimated input data to run the EQC model. EPA strongly recommends that the submitter use measured data, if available, to run the model. The use of estimated values as inputs introduces uncertainties that become magnified in modeling applications. In addition, the submitter indicated that "the relative distribution of substances within this category among environmental compartments will be evaluated using the Level I model." EPA recommends using the EQC Level III model from the Canadian Environment Modeling Centre at Trent University. This model can be found at the following Web address: http://www.trentu.ca/academic/aminss/envmodel/.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

EPA agrees with the submitter's proposal that adequate testing for the HPV Challenge Program purposes has been conducted for the alkaryl sulfonates for acute toxicity and genetic toxicity.

Comments on the adequacy of data for specific health effects endpoints are provided below. These

comments assume that the submitter will provide an adequate justification for the category approach as discussed in the category justification section.

Acute Toxicity. Well-conducted OECD guideline studies are available for 8 of the 12 category members and for one non-category structural analog. Because an upward trend in toxicity was not observed with increasing chain length, the submitter proposes to use data for CAS No. 115733-09-0 (C_{14}–C_{24} alkaryl calcium salt derivative) to fill the data gaps for untested materials. This plan is acceptable and no additional testing is necessary.

Repeated-Dose Toxicity. Robust summaries were submitted for five OECD guideline studies on two category members and one structural analog. These included dermal, inhalation, and oral exposure studies in rats and a dermal exposure study in rabbits. A limitation of the existing data for repeated-dose toxicity is the availability of only one oral exposure study, conducted on an non-category analog. However, the submitter plans to conduct an oral repeated-dose toxicity test on CAS no. 115733-09-0 (C_{14}–C_{24} alkaryl calcium salt derivative) as a range-finding study for a proposed reproductive toxicity test (see below). The proposed test substance, C14-C24 alkaryl calcium salt derivative (CAS No. 115733-09-0), was selected because it contains the highest proportion of fractions with the shortest alkyl chain length in the category (which are expected to have the greatest ability to penetrate biological membranes and reach potential toxicity targets based on arguments presented in Section 4.3.1 of the test plan). The combined oral toxicity data are expected to be representative of the structural diversity of the category. EPA therefore considers that the proposed Test Plan is adequate to address this endpoint, and no additional testing is necessary beyond that proposed by the submitter.

Genetic Toxicity. Four category members or analogs were tested for mutagenic potential and three were tested for chromosome aberration potential. The results obtained for each endpoint category were consistently negative. These data address the endpoint adequately and no additional testing is necessary.

Reproductive and Developmental Toxicity. The submitter's proposed one-generation test (OECD Test Guideline 415) using C_{14-24} alkaryl calcium salt (CAS no. 115733-09-0) to characterize reproductive and developmental toxicity is acceptable, if the submitter provides a more detailed discussion of similarity in physicochemical and toxicokinetic properties that demonstrates that the data obtained will adequately represent the reproductive and developmental toxicity of the category. If the submitter is unable to provide an adequate justification, testing of other category members may be necessary for this endpoint.
Ecotoxicity.

EPA disagrees with the submitter's plan to conduct WAFs testing, and believes that all aquatic testing should be done at the representative chemicals' aqueous dispersibility limit or at concentration of 1000 mg/L, whichever is lower. EPA suggests that the remaining chemicals be tested to quantify their dispersibility in water. Testing the most water-dispersible chemicals first may limit the need for further testing for aquatic toxicity. In addition, EPA also regards acute toxicity testing on all three species as unnecessary in this case and instead recommends that the fish acute toxicity testing be conducted first. If no effects are seen in this test, EPA proposes conducting daphnid chronic tests.

Specific Comments on the Robust Summaries

Health Effects.

The submitted summaries were well-prepared and adequately detailed, with the following exceptions: numerical summary data were rarely provided for study results and the sources of study data were not adequately documented in any of the summaries. Inclusion of summary data for treatment-related effects would assist reviewers in evaluation of the studies. For study references that are listed as "unpublished", the submitter needs to include the following information in the robust summary: the name of the laboratory

conducting the study; the study submitter; the title of the study; and the reference number of the study report.

A limitation noted for many of the summarized studies was lack of information on the composition and/or purity of the test material. Reported values for purity ranged from 35.1% ("active in oil", as described in the test plan) to 100% in the few cases where this information was reported.

Ecotoxicity.

All of the submitted studies employed WAFs. WAFs studies are not useful for risk assessment[1] of these chemicals. Water dispersibility concentrations were not determined or used for testing any of the chemicals of this category. The TOCs in these tests were above the required < 2.0 mg/L level. EPA recommends that prior to conducting more testing, the submitter should consider in its entirety Section 3. "Media Preparation and Exposure Systems" for difficult to test substances and elsewhere in Ref. 1. EPA emphasizes that the robust summaries for all proposed studies should be explicit in reporting of methods, procedures, and results.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

Reference

1.Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures, OECD, June 2000, Paris, France. OECD Environmental Health and Safety Publications, Series on Testing and Assessment, No. 23.